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| 10/578,946 | 02/05/2007 | John SantaLucia | DNASO-10963 | 5250 |
| 72960 | 7590 | 09/14/2011 | EXAMINER | |
| Casimir Jones, S.C. 2275 DEMING WAY, SUITE 310 MIDDLETON, WI 53562 | | | DEJONG, ERIC S | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|--|--|
| Office Action Summary | Application No. 10/578,946 | Applicant(s) SANTALUCIA ET AL. | |
| | Examiner ERIC S. DEJONG | Art Unit 1631 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 June 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 3-6 is/are pending in the application.
- 5a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 3-6 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED OFFICE ACTION

Applicants response filed 06/21/2011 is acknowledged.

Election/Restrictions

Applicant's election without traverse of Group II (claims 3-6) in the reply filed on 10/14/2010 is acknowledged.

Claims 1, 2, and 7-10 have been cancelled by applicant. Claims 3-6 are pending and currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 4, and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is newly applied and necessitated by applicants amendment to the instant claim.

Independent claim 3 has been amended to now recite "wherein said energy minimization algorithm comprises..." (see lines 13-39). Similarly, Independent claim 4

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has been amended to now recite a processor configured to carry out generalized computational process that also requires the same “energy minimization algorithm” as set forth in claim 3. Upon review the instant specification does not disclose nor describe any algorithm that comprises the generalized computational process steps recited in lines 15-29 of instant claim 3.

Independent claim 6 has been amended and is expressly read on a method that requires the use of “a configured processor” to carry out a carry out generalized computational process steps involving the decomposition of physical structure information, data association, candidate structure comparisons based on existing motifs, and the identification of unique structures. Upon review the instant specification does not disclose nor describe any “configured computer” nor the accompany program requisite for carrying out generalized computational process steps as recited in lines 4-15 of instant claim 6.

Claim Rejections - 35 USC § 112

The previous grounds rejection of 4 and 6 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of amendments made to the instant claims.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 4, and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is newly applied and necessitated by applicants amendment to the instant claims.

Independent claim 3 has been amended to now recite “wherein said energy minimization algorithm comprises...” (see lines 13-39). Similarly, Independent claim 4 has been amended to now recite a processor configured to carry out generalized computational process that also requires the same “energy minimization algorithm” as set forth in claim 3. Upon review the instant specification does not disclose nor describe any algorithm that comprises the generalized computational process steps recited in lines 15-29 of instant claim 3.

Therefore, the metes and bounds of independent claims 3 and 4 are indefinite because it cannot be determined what algorithm and/or requisite computational process steps are encompassed and excluded by the instant claims.

Independent claim 6 has been amended and is expressly read on a method that requires the use of “a configured processor” to carry out a carry out generalized computational process steps involving the decomposition of physical structure information, data association, candidate structure comparisons based on existing

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motifs, and the identification of unique structures. Upon review the instant specification does not disclose nor describe any “configured computer” nor the accompany program requisite for carrying out generalized computational process steps as recited in lines 4-15 of instant claim 6.

Therefore, the metes and bounds of independent claim 6 is indefinite because it cannot be determined what program or requisite computation steps are required to carrying out generalized steps recited in lines 4-15 of instant claim 6.

Claim Rejections - 35 USC § 103

The rejection of claim 3 35 U.S.C. 103(a) as being unpatentable over Floudas et al. (US Patent No 6,832,162) in view of Maier et al. (Eur Biophys K Biophys LETT (1999), see citation #27 of IDS filed 04/28/2010) has been withdrawn in view of the new grounds of rejection under 35 USC 112, 2nd paragraph set forth above.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Floudas et al. (US Patent No 6,832,162) in view of Maier et al. (Eur Biophys K Biophys LETT (1999), see citation #27 of IDS filed 04/28/2010).

In the instant case, the claimed invention is directed to a system for predicting nucleic acid three dimensional structure comprising a configured processor. The processor is configured to computer a plurality of secondary structures of a test nucleic acid, decompose said secondary structures into nucleic acid structure motifs, ranking said motifs into a hierarchal tree, identifying candidate three-dimensional motif structures from a database, linking said structural motifs to generate a candidate three-dimensional composite structure, refining said composite structures using an energy minimizing algorithm, ranking one or more candidate structures based on calculated energy and (optionally) by one or more scoring parameters based on of solvent accessible surface area, molecular density, and non-bonded energy, and selecting a refined candidate based on best calculated energy. Further, claim 5 is directed to a system comprising a configured processor for generating a nucleic acid structural motif database comprising only the steps of receiving nucleic acid physical structure information, decomposing said information into nucleic acid structural motifs, associating the data with said structure motifs, comparing structures to existing motifs in said database, and adding sad structure to said database.

Floudas et al. is sets forth the method and related systems of an *ab initio* prediction of α helices, β sheets, and polypeptide structures (see Abstract). The disclosed *ab initio* prediction approach involves 4 stages (See Figure 1 and col. 2, line 20 through col. 6, line 21). The first and second stages of the approach involve partitioning of the amino acid sequence of a protein of interest into a plurality of oligopeptides followed by the computation of secondary structure motifs therefrom (see

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col. 2, lines 20-60 and col. 11, lines 17-57). Floudas et al. further teaches, regarding the prediction of the folded state of a protein and how the formation of secondary structure and tertiary structure proceeds (see col. 5, line 61 through col. Col. 6, line 11), the classical approach of hierarchical folding, wherein secondary structural elements form rapidly followed by the slower arrangement of the tertiary fold. Floudas et al. further teaches that this approach is relied upon for the generation of α -helical secondary structure motifs (see col. 6, lines 3-11). Floudas et al. further teaches that the identification the three dimensional structure of secondary structure motifs based on the three-dimensional structures and properties of α -helices, β -sheets, and other known secondary structures common in protein structure (see col. 4, line 66 through col.5, line 10). Floudas et al. further teaches the linking of candidate secondary structures, using a hierarchal approach, to generate composite three dimensional structures by use of global optimization framework based on energy minimization (see col. 5, line 11 through col. 6, line 11).

While Floudas et al. teaches the above *ab initio* approach to the prediction of three-dimensional protein structure based on hierarchal linking of the tertiary structure of protein secondary motifs, Floudas et al. does not expressly teach or suggest the application of the *ab initio* prediction approach to the prediction of nucleic acid tertiary structures based on hierarchal linking of the tertiary structure of nucleic acid secondary motifs.

Maier et al. is relied upon for teaching that the use of conformational search methods used to predict biomolecular structure, encompass application to both protein

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and nucleic acid structure (see Maier et al., page 565, col. 1, lines 25-59). Maier et al. further teaches that the progress achieved in the predicting biomolecular structure is documented by successful applications to searching conformational space of oligopeptides (non-nucleic acids). Maier et al. further teaches that the remarkable intrinsic stability of certain classes of RNA structural motifs play an important role in the tertiary folding of RNA molecules and the emerging "tool-kit" of RNA structural motifs is expected to substantially aid in the model building of RNA 3D structures (see Maier et al., page 565, lines 1-24).

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to modify the *ab initio* modeling approach to prediction of protein three dimensional structure prediction, as taught by Floudas et al., to accommodate the prediction of nucleic acid three dimensional computing and identifying the three dimensional structure of nucleic acid secondary structure motifs, as taught by Maier et al., in place of the three dimensional structure of protein secondary structure motifs. One of ordinary skill in the art would recognize from the teachings of Maier et al. that computational modeling and prediction approaches of biomolecules can accommodate either nucleic acid and protein structures. Further one of skill in the art would rely upon the teachings of Maier et al. in the computation, ranking and identification of nucleic acid secondary structural motifs and their three dimensional structure.

Response to Arguments

Applicant's arguments filed 06/21/2011 have been fully considered but they are not persuasive.

With regard to the rejection of claim 5 under 35 U.S.C. 103(a) as being unpatentable over Floudas et al. (US Patent No 6,832,162) in view of Maier et al. (Eur Biophys K Biophys LETT (1999), see citation #27 of IDS filed 04/28/2010), applicants argue that a processor configured to execute the steps recited in claim 5, or a method making use of the process steps.

In response, the examiner emphasizes that the instant rejection is not an anticipatory rejection under 35 USC 102, but rather a rejection based on obviousness under 35 USC 103. Applicant's argument further does not appear to take into consideration that all the computational modeling set forth in both Maier et al. and Floudas et al. was done entirely on computer. Therefore, applicants arguments are not persuasive.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ERIC S DEJONG/
Primary Examiner, Art Unit 1631